REMARKS

The claims have been amended to clarify the invention. Claim 2 has been amended at to recite a polynucleotide comprising SEQ ID NO:4, a polynucleotide encoding SEQ ID NO:6, and a naturally occurring variant of SEQ ID NO:4 having at least 95% identity to SEQ ID NO:4 and to claim the complement of all recited polynucleotides of a)-c) in the preamble of the claim. Claim 4 has been amended at clause (b) to recite "an immunogenic fragment" of SEQ ID NO:6 having at least 6 sequential amino acids of SEQ ID NO:6, and to delete the recitation of variant polypeptide sequences. Support for the amendment to 4 citing an immunogenic fragment of SEQ ID NO:6 is found in the specification, for example, at p. 4, lines 3-5 and means of identifying said fragments are described in the specification at p. 26, lines 29-33. No new matter is added by these amendments, and entry of the amendments is therefore requested.

35 U.S.C. § 132, Objection to Claims 2 and 4

The Examiner has objected to the amendments to claims 2 and 4 filed December 10, 2002, because it introduces new matter to the disclosure. The Examiner stated the new matter which is not supported by the original disclosure is (a) that portion of the subject matter described by clause (d) of claim 2 which is a naturally-occurring variant of the polynucleotide having at least 95% identity to an isocoding, or isocomplementary polynucleotide of clause (b) and (c), and (b) the subject matter described in clause (c) of claim 4.

The Examiner stated that the specification provides no support for a specific amount of 5% divergence in a polynucleotide that is isocoding or isocomplementary to a nucleotide sequence of SEQ ID NOs:1-5 but only to a polynucleotide sequence of SEQ ID NOs:1-5 (see specification, at page 8, lines 8-10). Further, the Examiner stated, the specification provides no support for a specific amount of 5% divergence in amino acid sequences of variants of the polypeptide of SEQ ID NO:6. Applicant is required to cancel the new matter in the reply to this office action.

Claim 2 has been amended at step c) to recite a 95% variant of only SEQ ID NO:4, and claim 4 has been amended to delete variant language. Withdrawal of the objection is therefore requested.

35 U.S.C. § 101, Rejection of Claims 2 and 4-8

The Examiner has maintained the rejection of claims 2 and 4-8 under 35 U.S.C. § 101 for reasons of record. The Examiner stated that applicant's arguments filed December 12, 2002 have been fully considered but are not persuasive for the following reasons. The Declaration under 37 CFR 1.132 is insufficient to overcome the rejection because it is incomplete. Applicants has not provided the journal article referenced in the Declaration, i.e., Thompson et al., Genomics Research, Vol. 12 pages 1517-1522. The Examiner, however, made certain observations to the extent that the Declaration's paragraph addresses the specification's disclosure.

1) It is noted that the arguments of Paper No. 12 and the statements in the Declaration posit no potential utility for subject matters of the broad genus of products described by clause (b) and in part by clause (c), of claim 2 and the even broader product genus described by clause (d) of claim 2. Likewise, the arguments of Paper No. 12 and statements in the Declaration posit no potential utility for subject matters of the broad genera of products described in clauses (b) and (c) of claim 4 and do not directly discuss potential utility for the product described by clause (a) of claim 4.

Applicants Response

Applicants apologize for the inadvertent omission of the Thompson reference intended to accompany the declaration in the previous response and herewith submit with this response, the omitted reference. Applicants disagree that the arguments and declaration presented in the previous response do not directly address potential utility for the elements in claims 2 and 4, as presently amended. Applicants arguments, and the Walker declaration, specifically address the utility of polynucleotide encoding SEQ ID NO:6, i.e., SEQ ID NO:4, the subject matter of clause (b) of claim 2, as well as its encoded polypeptide, the subject matter of clause (a) of claim 4. The Walker declaration first describes the relevant points of the Thompson article in ¶5 of the declaration regarding the use of GBA analysis (as in the instant application) to identify functionally associated molecules by their coexpression and the identification of disease associations within these modules. The Walker declaration then describes in ¶ 7 of the declaration the use of the same (GBA) method in the instant application to identify a functional module of genes, including SEQ ID NO:4, associated with neurotransmitter processing and neurological disorders, in particular, with Parkinson's disease, schizophrenia, and neuroendocrine

cancers and posits the use of the claimed polynucleotides "in particular SEQ ID NO:4 and its encoded protein, SEQ ID NO:6, in the diagnosis or in monitoring the progress of therapeutic intervention for diseases associated with neurotransmitter processing, in particular, with Parkinson's disease, schizophrenia, and neuroendocrine cancers" (Walker declaration at p. 3). Based on the asserted uility for SEQ ID NO:4 and its encoded polypeptide, the use of variants of the polynucleotide sequence, as recited in clause (c) of claim 2, in hybridization studies to distinguish between SEQ ID NO:4 and closely related polynucleotides is clearly useful (see specification, at p. 8, line 26 through p. 9, line 6). Likewise the use of fragments of the polypeptide, as recited in clause (b) of claim 4 for the production and use of antibodies to SEQ ID NO:6 to identify SEQ ID NO:6 and for use in competitive protein binding assays is clearly apparent from the specification (see specification, at pp. 14 and 26-27).

2) Neither the arguments of Paper No. 12 nor any paragraph of the declaration of Paper 11 contest or contradict the finding of Paper No. 10, mailed September 23, 2002, that no prior art polypeptide having a known or proposed function shares any significant homology with the polypeptide of SEQ ID NO:6. Consequently, the putative association the declaration reports in paragraphs 6(e) -6(g) (sic, 5(e)-5(g)), to have been made in the absent article of Thompson et al. is unavailable on the present record. No interaction can be attributed to a polypeptide of SEQ ID NO:6, or a mRNA transcript having a nucleic acid sequence of SEQ ID NO:4 present in a nerve cell, with any other polypeptide contemporaneously expressed by, or transcript present in, human nerve cells. Applicants arguments of Paper No. 12 and the declaration's statements, contemplate a twice-removed "guilt-by-association analysis": guilt-by-association of a transcript encoding a product of no known function in 12 cDNA libraries, see page 24 of the specification, to two products guilty-by-association with certain disorders.

Applicants Response

The Thompson article is hereby submitted with the present response and is therefore of record. The associations made in the Walker declaration, specifically in ¶¶ 5 and 7, have been discussed above in response to item (1). The "substantial likelihood" of a functional association between SEQ ID NO:4 and four other genes associated with neurotransmitter processing and certain neurological disorders is therefore established by the results of the Thompson study and the arguments of Paper No. 12 and the declaration's statements presented above. The likely

functional association of SEQ ID NO:6 with neurotransmitter processing and associated neurological disorders is made without the need for any particular sequence homology with any protein of known function based on the findings of the Thompson article establishing that functional association may be made based on coexpression and the fact that the polynucleotide encoding SEQ ID NO:6 is highly significantly coexpressed with four known genes that function in neurotransmitter processing.

3) Neither the gene transcribed as a nucleic acid sequence corresponding to SEQ ID NO:4 herein, nor its encoded product of SEQ ID NO:6 herein, are shown to have any association with upregulation of neurotransmitter gene expression or downregulation of such gene expression, nor association with the modulation of cellular response to any neurotransmitter or processing any neurotransmitter, nor association with any other nerve cell activity. This is because there is no negative control in the specification that might indicate that levels of expression of products of SEQ ID NO:4 and/or SEQ ID NO:6 differ in normal central nervous system from their expression levels in, e.g., neuronal precursor cells or in neurons that contribute to a medical condition or disease as indicated in the declaration. Thus, the specification when combined with the declaration is not seen to establish any specific and substantial association, or prospective utility for the elected subject matter .... particularly in the absence of the referenced article.

Applicants Response

The specification makes no claim to the utility of the claimed polynucleotides based on direct mesurements of differential gene expression data. The Thompson article specifically establishes the use of the GBA method of Walker et al. (Thompson article, P. 1518) as an alternative to microarray studies to establish modules of gene expression that are functionally related based on coexpression in both normal and diseased tissues as well as their likely disease associations (Thompson article, p. 1517 bridging p. 1518). In so doing, the Thompson article provides independent confirmation for the previous use of the Walker GBA method in the instant application to identify previously unknown genes represented by SEQ ID NOs:1-5 that are highly significantly coexpressed with a known functional module of genes involved in neurotransmitter processing and also associated with various neurological diseases and disorders. It is this association that provides a substantial likelihood for the use of the claimed polynucleotides, SEQ ID NOs:1-5 and/or their encoded polypeptides as additional markers in the diagnosis or in

monitoring the progress of therapeutic intervention for diseases associated with neurotransmitter processing. For example, it is substantially likely that a gene microarray including these polynucleotide sequences would be more useful then one that did not contain them in connection with the use of a microarray in diagnosing or monitoring therapeutic intervention for such diseases.

Moreover, the Office Action has ignored the fact that the recited polynucleotides and encoded polypeptides have specific, substantial, and credible utilities in, for example, toxicology testing in drug discovery, in particular, drug discovery related to the treatment of diseases associated with neurotransmitter processing such as those discussed above. One of skill in the art would know that, as a part of such toxicology testing, the recited polynucleotides could be used to detect toxic side effects of drug candidates targeted to a particular polypeptide in terms of their effects on the expression of other genes and their encoded polypeptides using any of a number of methods well known in the art for studying differential gene expression, in particular, in a microarray format. See, in particular, the specification, at p. 5, lines 27-31, and at p. 13, lines 29-33. Therefore, the claimed polynucleotides meet the utility requirement of 35 U.S.C. § 101 based at least on the well-known, specific, and substantial utilities of expressed, naturally occurring polynucleotides in toxicology testing and drug discovery. Withdrawal of the rejection of claims 2 and 4-8 under 35 U.S.C. § 101 is therefore requested.

35 U.S.C. 112, First Paragraph, Rejection of Claims 2 and 4-8

The Examiner has rejected claims 2 and 4-8 under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, for applicants reasons set forth above, it should be withdrawn for the same reasons.

The Examiner has also rejected claims 2 and 4-8 under 35 U.S.C. 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The Examiner stated that this rejection differs from that stated in Paper No. 10 in that it addresses in part the amendments of Paper No. 12 to clause (d) of claim 2 and clause (c) of claim 4 as well as clause (b) of claim 2 (sic, 4?), which is not necessitated by applicants amendments. The specification fails to exemplify or describe the design, preparation, or isolation of nucleic acid sequence products of amended clause (d) of claim 2 that diverge in their coding capacity from the elected sequence of SEQ ID NO:4. The specification also fails to exemplify or describe the design, preparation, or isolation of polypeptide products of clause (b) and the amended clause (c) of claim 4 that diverge in their amino acid sequence from that set forth in SEQ ID NO:4 (sic,6). The Examiner cited *Fiers V. Revel* with respect to the principle that "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112.

The Examiner stated that the specification nowhere identifies any specific structural characteristic of the polypeptide having the amino acid sequence of SEQ ID NO:6, not does it provide any informational characteristic of a nucleic acid encoding the amino acid sequence of SEQ ID NO:6 that would permit a correlation between either of these products and any of the divergent products statistically described in the amendments to clause (d) of claim 2 and of clause (c) of claim 4. Neither does the specification identify further structural characteristics of any polypeptide of clause (b) of claim 4 that comprises six contiguous amino acids of SEQ ID NO:6 other than SEQ ID NO:6 itself. Nothing demonstrates that, at the time the application was filed, applicant was "able to envision" enough of the structure of claimed, divergent, products to provide the public with identifying characteristics [that could] sufficiently demonstrate to skilled artisans that applicant possessed the claimed subject matter. Fiers, 35 USPQ2D at 1604 (citing Amgen, Inc v. Chugai pharmaceutical Co., 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The Examiner stated that deleting claim 2's clause (d) and claim 4's clauses (b) and (c) will avoid the rejection.

Applicants response

The rejection of claims 2 and 4-8 under 35 U.S.C. 112, first paragraph is respectfully traversed for the following reasons:

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law, some of which has been cited by the Examiner in the rejection.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

SEQ ID NO:4 and SEQ ID NO:6 are specifically disclosed in the application (see, for example, page 3, lines 24-26). Variants of SEQ ID NO:4 are described, for example, at page 3, lines 27-33. In particular, the preferred, more preferred, and most preferred variants (70%, 85%, and 95% nucleic acid sequence similarity to SEQ ID NO:4) are described, for example, at 8, lines 8-10. Chemical and structural features of the polypeptide (SEQ ID NO:6) encoded by the polynucleotide of SEQ ID NO:4 are described, for example, on page 25, lines 9-15 of the specification. Given SEQ ID NO:4, one of ordinary skill in the art would recognize naturally-occurring variants of SEQ ID NO:4 having 95% sequence identity to SEQ ID NO:4. Accordingly, the Specification provides an adequate written description of the recited polynucleotide sequence.

A. The Specification provides an adequate written description of the claimed "variants" of SEQ ID NO:4.

The Office Action has further asserted that the claims are not supported by an adequate written description because

> The specification fails to exemplify or describe the design, preparation, or isolation of nucleic acid sequence products of amended clause (d) of claim 2 that diverge in their coding capacity from the elected sequence of SEQ ID NO:4
>
> (page 8 of the Office Action of 3/05/2003)

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides or polypeptides in terms of chemical structure, rather than on functional characteristics. For example, the "variant language" of independent claim 2 recites chemical structure to define the claimed genus:

> 2. A substantially purified polynucleotide ... comprising a polynucleotide sequence selected from: (a) a polynucleotide sequence of SEQ ID NO:4; ... and (c) a naturally-occurring variant of the polynucleotide of (a), having at least 95% identity to the polynucleotide sequence of (a).

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:4. In the present case, there is no reliance merely on a description of functional characteristics of the polynucleotides recited by the claims. In fact, there is no recitation of functional characteristics. Moreover, if such functional recitations were included, it would add to the structural characterization of the recited polynucleotides. The polynucleotides defined in the claims of the present application

recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*

2. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those case was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of August 26, 1999. Much has happened in the development of recombinant DNA technology in the 20 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:4 and SEQ ID NO:6, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide variants at the time of filing of this application.

3. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is

defined in terms of the chemical structure of SEQ ID NO:4 or SEQ ID NO:6. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides defined by the present claims is adequately described, as evidenced by consideration of the claims of the '740 patent involved in *Lilly*. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

B. The Specification provides an adequate written description of the claimed "fragments" of SEQ ID NO:6.

Applicants disagree that the specification does not identify further structural characteristics of any polypeptide of clause (b) of claim 4, as amended, other than the amino acid sequence of SEQ ID NO:6. The specification describes fragments of the polypeptide of SEQ ID NO:6 in the specification at p. 4, lines 3-5; "which are preferably at least 5 to15 amino acids in length ... and which retain some biological activity or immunological activity of, for example, SEQ ID NO:6. The specification also describes various structural motifs within the polypeptide sequence of SEQ ID NO:6, at p. 25, lines 9-15, and further describes well known methods of identifying suitable immunogenic fragments within the polypeptide sequence of SEQ ID NO:6 at p. 26, lines 29-33. Given SEQ ID NO:6, as well as these descriptions of fragments of SEQ ID NO:6, one skilled in the art could readily envision any and all such fragments of SEQ ID NO:6 comprising at least 6 sequential amino acids of SEQ ID NO:6 and which retain immunogenic activity.

With the amendments to claim 4 deleting clause (c) and reciting an immunogenic fragment of SEQ ID NO:6 in clause (b) of claim 4, applicants submit that one skilled in the art would readily recognize applicants possession of the claimed variants of SEQ ID NO:4 as recited in clause (c) of claim 2, as well as the claimed fragments of SEQ ID NO:6, as recited in clause (b) of claim 4. Withdrawal of the rejection of claims 2 and 4-8 under 35 U.S.C. § 112, first paragraph is therefore requested.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 2 and 4-8

The Examiner has rejected claims 2 and 4-8 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for designing a nucleic acid sequence encoding the polypeptide of SEQ ID NO:6, and for preparing the encoded polypeptide, does not reasonably

provide enablement for a nucleic acid sequence encoding a polypeptide having an amino acid sequence differing from that set forth in SEQ ID NO:6, or from a polypeptide differing from that set forth in SEQ ID NO:6.

The Examiner stated that this rejection differs from that stated in Paper No. 10 in that it addresses in part the amendments of Paper No. 12 to clause (d) of claim 2 and clause (c) of claim 4 as well as clause (b) of claim 2 (sic, 4?), which is not necessitated by applicants amendments. With the amendments to claims 2 and 4, the claims now contemplate, in part, arbitrary alterations of the nucleic acid sequence encoding SEQ ID NO:6 at as many as 10 amino acid positions without any teaching suggesting where, and how, the amino acid sequence or encoding nucleic acid sequence may be altered. Clause (b) of claim 4 additionally contemplates arbitrary alteration, e.g., removal of up to 97% of the amino acid sequence of SEQ ID NO:6 wherein the remaining 3% of the amino acid sequence may be a hexapeptide that occurs anywhere in SEQ ID NO:6. The Examiner stated that there is no basis in the specification for either the lesser or greater degree of amino acid sequence alteration, or corresponding codon alteration in the encoding nucleic acid because neither the prior art of record of applicant's specification can identify, taken together, any function of the polypeptide of SEQ ID NO:6. The Examiner further cited various court cases relative to the principle that "a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides". See page 11 of the Office Action. The Examiner concluded by stating that the present specification can provide no basis whatsoever for a functional definition of the disclosed product, and provided an application of the "Forman" factor (In re Wands) to applicants disclosure.

Applicants Response

The amendments to claims 2 and 4 limiting the claimed variant sequences to a polynucleotide sequence having at least 95% identity to the polynucleotide sequence of SEQ ID NO:4 have been discussed above. Further, applicants description of the claimed polynucleotide sequences in primarily structural terms have also been discussed above in response to the rejection of claims under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description, and these comments are incorporated by reference in response to the current enablement rejection. Applicants submit that a lack of any "functional definition" of the encoded protein, SEQ ID NO:6, is not limiting to the scope of enablement for the claimed polynucleotides. The specification discloses, and extensively references, methods of identifying variants of SEQ ID NOs:1-5 of the invention at p. 8, lines 11-25. The use of such a narrow scope

of variants of the polynucleotide sequence of SEQ ID NO:4 as claimed, i.e., one having at least 95% sequence identity to SEQ ID NO:4, in hybridization assays [such as those described at page 8, beginning at line 26] to distinguish between SEQ ID NO:4 and related polynucleotides would be clearly evident to one skilled in the art and is not dependent on any "functional definition" for the polynucleotide of SEQ ID NO:4 or its encoded polypeptide. Likewise, there is no necessity for any "functional definition" for any given hexapeptide fragment of SEQ ID NO:6 other than that it "retain some ... immunological activity of ... SEQ ID NO:6" as previously noted. Methods of making fragments of the polypeptide of SEQ ID NO:6 are also described in the specification at p. 11, lines 24-30.

The specification, coupled with that which is well known to one of skill in the art at the time the application was filed, thus clearly enables one of skill in the art to make and use the invention commensurate in scope of claims 2 and 4-8, particularly with regard to claim 2(c) and claim 4(b), and withdrawal of the rejection of claims 2 and 4-8 under 35 U.S.C. § 112, first paragraph is therefore requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited. Applicants further request that, upon allowance of claim 2, that claim 10 be rejoined as a method of use of the polynucleotides of claim 2 that depends from and is of the same scope as claim 2 in accordance with *in Re Ochiai* and the MPEP § 821.04. Applicants further request that, upon allowance of claim 2 and the composition of matter of SEQ ID NO:4, claims 12-14 also be rejoined as a combination containing SEQ ID NO:4 and its methods of use in accordance with the MPEP § 803.04.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,
INCYTE CORPORATION

Date: June 2, 2003

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